



Reduced susceptibility to polyenes associated with a missense mutation in the ERG6 gene in a clinical isolate of *Candida glabrata* with pseudohyphal growth.

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Titre	Reduced susceptibility to polyenes associated with a missense mutation in the ERG6 gene in a clinical isolate of <i>Candida glabrata</i> with pseudohyphal growth.
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Auteur	Vandeputte, Patrick [1], Tronchin, Guy [2], Bergès, Thierry [3], Hennequin, Christophe [4], Chabasse, Dominique [5], Bouchara, Jean-Philippe [6]
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Résumé en anglais	<p>Little information is available about the molecular mechanisms responsible for polyene resistance in pathogenic yeasts. A clinical isolate of <i>Candida glabrata</i> with a poor susceptibility to polyenes, as determined by disk diffusion method and confirmed by determination of MIC, was recovered from a patient treated with amphotericin B. Quantitative analysis of sterols revealed a lack of ergosterol and an accumulation of late sterol intermediates, suggesting a defect in the final steps of the ergosterol pathway. Sequencing of CgERG11, CgERG6, CgERG5, and CgERG4 genes revealed exclusively a unique missense mutation in CgERG6 leading to the substitution of a cysteine by a phenylalanine in the corresponding protein. In addition, real-time reverse transcription-PCR demonstrated an overexpression of genes encoding enzymes involved in late steps of the ergosterol pathway. Moreover, this isolate exhibited a pseudohyphal growth whatever the culture medium used, and ultrastructural changes of the cell wall of blastoconidia were seen consisting in a thinner inner layer. Cell wall alterations were also suggested by the higher susceptibility of growing cells to Calcofluor white. Additionally, complementation of this isolate with a wild-type copy of the CgERG6 gene restored susceptibility to polyenes and a classical morphology. Together, these results demonstrated that mutation in the CgERG6 gene may lead to a reduced susceptibility to polyenes and to a pseudohyphal growth due to the subsequent changes in sterol content of the plasma membrane.</p>

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